

# Non-Insulin Dependent Diabetes Mellitus: an Epidemic Among Hawaiians

Ralph Beddow, MD, FACP and Richard Arakaki, MD  
Department of Medicine, John A. Burns School of Medicine, University of Hawaii-Manoa

## The Problem in America

An estimated 14-15 million people in the United States have diabetes mellitus, and greater than 90 % have non-insulin dependent diabetes mellitus (NIDDM) or Type II Diabetes. One-half of the NIDDM cases are undiagnosed. Moreover, when diagnosed, NIDDM has probably been present for 4 to 7 years prior to diagnosis, based on the presence of long-term complications at the time of diagnosis. Diabetes prevalence has increased dramatically in the United States over the past 30 years by approximately 50 % every 7 years. The large increase is probably due to a shift in the age of the population as well as accurate ascertainment of disease. In the past decade, diabetes incidence in the United States has stabilized (40% increase since 1980), and is presently estimated at 650,000 new cases per year.<sup>1</sup> However, the incidence worldwide and especially in the developing countries is steadily rising. The World Health Organization (WHO) has concluded that the "apparent epidemic of diabetes occurring worldwide is strongly related to lifestyle and economic changes".

Current data from the Centers for Disease Control and Prevention and the National Center for Health Statistics reveal the staggering impact of diabetes and its complications in the United States. Diabetes is among the 10 leading causes of death, the underlying cause in over 40,000 deaths per year, and a contributing cause in perhaps another 30,000 deaths.<sup>2</sup> The majority of adults with NIDDM die from macrovascular disease which includes cardiovascular, cerebrovascular, or peripheral vascular disease. Among deaths related to diabetes, cardiovascular disease is the cause of more than 80,000 cases per year.<sup>3</sup> Diabetes is the primary diagnosis in almost 500,000 hospital discharges per year and the secondary diagnosis in almost 3 million hospitalizations in a year.

Diagnosed NIDDM is only the tip of the iceberg of an epidemic of glucose intolerance. Impaired glucose tolerance or IGT is even more prevalent than NIDDM. In addition to being a major risk factor for the development of NIDDM, IGT is associated with an increased risk for macrovascular disease. IGT is not associated with diabetes-specific complications of microvascular disease which includes retinopathy, nephropathy, and neuropathy. Among adults 20-74

years of age in the United States, estimates in 1990 and in accordance with WHO criteria, approximately 18% have some form of glucose intolerance (7% with NIDDM and 11% with IGT).<sup>1</sup> The major impact of aging is evidenced by the 42% prevalence of IGT and NIDDM in the population between 65 and 74 years. The risk of abnormal glucose tolerance is greatly increased in minority populations such as African Americans, Hispanic Americans, American Indians, Asian and Pacific Island Americans. On the basis of the continued growth of the fraction of the United States population older than 65 years, and of the ethnic and racial groups at particularly high risk of developing NIDDM and IGT, the overall prevalence of glucose intolerance is feared to increase in the next decade.

## The Epidemic Among Hawaiians

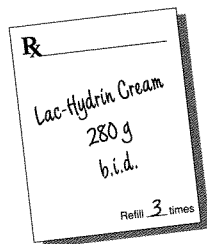
In 1985, a Medical Task Force Report, researched and prepared by E Ola Mau, a consortium of Native Hawaiian Health Professionals, reported "From 1910 to 1980, in every major disease category, pure Hawaiians had the highest mortality rate. Rates for part Hawaiians were intermediate or similar to those for all races".<sup>4</sup> This report led to the enactment of the Native Hawaiian Health Care Act signed into law by President Ronald Reagan in 1988 which provides for resources to improve the health status of Hawaiians.

The comparison of diabetes mellitus rates among Native Hawaiians and other races in Hawaii had been initially reported by Sloan in 1963.<sup>5</sup> Of 38,103 adults employed on Oahu, pure Hawaiians had a prevalence rate for diabetes of 48.8 per 1000 individuals as compared to a rate of 18.4 per thousand of all races. Part Hawaiians were found to have an intermediate rate of 26.6 diabetics per thousand. In 1966, a study conducted on the island of Niihau had identified 8 diabetics among 60 pure Hawaiian men, a prevalence rate of 12%.<sup>6</sup> The Molokai Heart Study had examined 247 adult Hawaiians between the ages of 20 to 59 on the island of Molokai, and reported a diabetes prevalence rate of 10% in women and 12% in men.<sup>7</sup> Most recently, the Native Hawaiian Health Research Project, a descriptive epidemiologic study of diabetes and heart disease risk factors among Native Hawaiians, have reported the highest prevalence rate of diabetes to date. In 1993, this University of Hawaii sponsored project examined with a 2 hour Oral Glucose Tolerance Test (OGTT) 177 adult Hawaiians over the age of 30 years residing in North Kohala. A diabetes prevalence rate of 18 % by WHO criteria was observed.<sup>8</sup> The combined results of all these studies clearly document the increasing rate of diabetes among Native Hawaiians over the past 30 years. As compared to the national trend, the prevalence rate is higher, and appears to be disproportionately increasing over 3 decades (Figure 1).

The Native Hawaiian Health Research Project has also reported an IGT rate of 16 % (Fasting Blood Glucose < 140 mg/dl, and a 2 hour value between 140-199 mg/dl during an OGTT, WHO criteria), the first assessment of IGT prevalence among Hawaiians. The

Address correspondence to:  
Richard Arakaki MD  
Department of Medicine  
1356 Lusitana Street  
7th Floor  
Honolulu, HI 96813  
Phone: (808) 586-2910  
Fax: (808) 586-7486

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**CAUTION:** Federal law prohibits dispensing without a prescription.

## Lac-Hydrin® 12%\* (ammonium lactate cream) Cream

For Dermatologic use only. Not for ophthalmic, oral or intravaginal use.

**DESCRIPTION:** \*Lac-Hydrin is a formulation of 12% lactic acid neutralized with ammonium hydroxide, as ammonium lactate, with a pH of 4.4-5.4. Lac-Hydrin Cream also contains water, light mineral oil, glyceryl stearate, polyoxyl 100 stearate, propylene glycol, polyoxyl 40 stearate, glycerin, cetyl alcohol, magnesium aluminum silicate, laureth-4, methyl and propyl parabens, methylcellulose, and quaternium-15. Lactic acid is a racemic mixture of 2-hydroxypropanoic acid and has the following structural formula:



**CLINICAL PHARMACOLOGY:** Lactic acid is an alpha-hydroxy acid. It is a normal constituent of tissues and blood. The alpha-hydroxy acids (and their salts) are felt to act as humectants when applied to the skin. This property may influence hydration of the stratum corneum. In addition, lactic acid, when applied to the skin, may act to decrease corneocyte cohesion. The mechanism(s) by which this is accomplished is not yet known.

An *in vitro* study of percutaneous absorption of Lac-Hydrin Cream using human cadaver skin indicates that approximately 6.1% of the material was absorbed after 68 hours.

**INDICATIONS AND USAGE:** Lac-Hydrin Cream is indicated for the treatment of ichthyosis vulgaris and xerosis.

**CONTRAINDICATIONS:** None known.

**WARNING:** Use of this product should be discontinued if hypersensitivity to any of the ingredients is noted. Sun exposure (natural or artificial sunlight) to areas of the skin treated with Lac-Hydrin Cream should be minimized or avoided (see Precautions section).

**PRECAUTIONS: General:** For external use only. Stinging or burning may occur when applied to skin with fissures, erosions, or that is otherwise abraded (for example, after shaving the legs). Caution is advised when used on the face because of the potential for irritation. The potential for post-inflammatory hypo- or hyperpigmentation has not been studied.

**Information for patients:** Patients using Lac-Hydrin Cream should receive the following information and instructions:

1. This medication is to be used as directed by the physician, and should not be used for any disorder other than for which it was prescribed. Caution is advised when used on the face because of the potential for irritation. It is for external use only. Avoid contact with eyes, lips, or mucous membranes.
2. Patients should minimize or avoid use of this product on areas of the skin that may be exposed to natural or artificial sunlight, including the face. If sun exposure is unavoidable, clothing should be worn to protect the skin.
3. This medication may cause stinging or burning when applied to skin with fissures, erosions, or abrasions (for example, after shaving the legs).
4. If the skin condition worsens with treatment, the medication should be promptly discontinued.

**Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis:** A long-term photomutagenicity study in hairless albino mice suggested that topically applied 12% ammonium lactate cream enhanced the rate of ultraviolet light-induced skin tumor formation. Although the biologic significance of these results to humans is not clear, patients should minimize or avoid use of this product on areas of the skin that may be exposed to natural or artificial sunlight, including the face. Long-term dermal carcinogenicity studies in animals have not been conducted to evaluate the carcinogenic potential of ammonium lactate.

**Pregnancy: Teratogenic effects: Pregnancy Category C.** Animal reproduction studies have not been conducted with Lac-Hydrin Cream. It is also not known whether Lac-Hydrin Cream can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Lac-Hydrin Cream should be given to a pregnant woman only if clearly needed.

**Nursing Mothers:** Although lactic acid is a normal constituent of blood and tissues, it is not known to what extent this drug affects normal lactic acid levels in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lac-Hydrin Cream is administered to a nursing woman.

**Pediatric Use:** The safety and effectiveness of Lac-Hydrin Cream have not been established in pediatric patients less than 12 years old. Potential systemic toxicity from percutaneous absorption has not been studied. Because of the increased surface area to body weight ratio in pediatric patients, the systemic burden of lactic acid may be increased.

**ADVERSE REACTIONS:** In controlled clinical trials of patients with ichthyosis vulgaris, the most frequent adverse reactions in patients treated with Lac-Hydrin Cream were rash (including erythema and irritation) and burning/stinging. Each was reported in approximately 10-15% of patients. In addition, itching was reported in approximately 5% of patients.

In controlled clinical trials of patients with xerosis, the most frequent adverse reactions in patients treated with Lac-Hydrin Cream were transient burning, in about 3% of patients, stinging, dry skin and rash, each reported in approximately 2% of patients.

**DOSAGE AND ADMINISTRATION:** Apply to the affected areas and rub in thoroughly. Use twice daily or as directed by a physician.

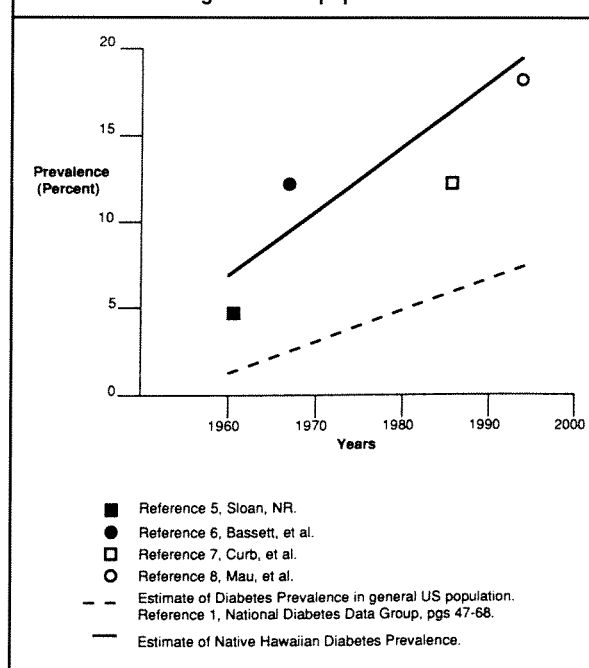
**HOW SUPPLIED:** Lac-Hydrin Cream is available in cartons of 280 g (2-140 g plastic tubes). Store at controlled room temperature, 15-30°C (59-86°F).



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03-5982-1  
Revised August 20, 1996

**Fig 1.—Prevalence estimates of diabetes mellitus in Native Hawaiians and the general U.S. population from 1960 - 1996.**



IGT rate appears to equal the rate of diabetes, which places the rate of glucose intolerance among Hawaiians at 34 % or one in three adult Hawaiians over the age of 30. This rate of glucose intolerance is alarmingly nearly twice the rate of 18 % observed for the general United States population. Importantly, this combined rate of NIDDM and IGT among Hawaiians significantly contributes to increased CVD risk and may remain the primary factor responsible for the observed increased heart disease morbidity and mortality. The identification of the IGT population offers a glimpse of future NIDDM prevalence and the opportunity to intervene.

In Hawaii, approximately 8% of the State population is estimated to have diabetes. Thus, in a State of about a million people, about 80,000 individuals have diabetes, primarily adults with NIDDM. Among Hawaiians, based on the recent data from the North Kohala community, approximately one of five adults have diabetes. The State of Hawaii's adult Hawaiian population over the age of 30 is estimated to be 100,000 or 50% of the total population of 200,000 people.<sup>9</sup> Thus, 20,000 adult Hawaiians have diabetes which account for approximately one fourth of the State's diabetic population. This is clearly a disproportionate and unfortunate representation. In addition, among dialysis patients with diabetes, over 40% are Native Hawaiians which suggest an increased rate of diabetic complications among Hawaii's indigenous population.

## Efforts to Prevent Diabetes and Diabetes-Related Complications

Despite the putative role for genetic factors in its development, NIDDM may be largely preventable. Studies have demonstrated the adverse consequences of decreased physical activity and obesity, and the risk for developing NIDDM. These observations support the

role of potentially reversible factors in the development of diabetes. Among the most important factors associated with increased risk of developing NIDDM are obesity, age greater than 40 years, a history of IGT or gestational diabetes mellitus (GDM), a positive family history of NIDDM, and being a member of a minority population. These many risk factors are also associated with IGT. Approximately, 30-40 % of IGT individuals progress on to NIDDM over a 5-10 year period. The rate of progression is estimated to be approximately 5 % per year and may be greater among higher risk populations. Women with GDM also have an approximate 10 year risk of 30-40 % for developing NIDDM. In recently industrialized countries and in migrating populations that previously had a low prevalence of NIDDM, changes in diet and an increasingly sedentary lifestyle, with consequent increase in body mass, have been associated with the development of NIDDM. It is apparent that the "epidemic of diabetes" may worsen in the future, and the need to intervene is overwhelming.

Still, we can take heart in a number of advances and new initiatives that may reduce the rate of NIDDM and diabetes-related complications in the future. The Diabetes Control and Complications Trial, a landmark study reported in 1993, has shown that lower blood glucose levels either prevent or decrease diabetic eye and kidney diseases.<sup>10</sup> Subsequently, many more studies have come to emphasize the relationship of lower blood glucose concentrations and reduced rates of complications among all diabetics. Thus, it is apparent that measures to improve blood glucose control among Hawaiians and all races with diabetes should reduce long-term complications. There are now many new options for the treatment of diabetes which includes new anti-hyperglycemic agents, multidisciplinary approaches to diabetes care, and easier means to monitor blood sugars and disease progression. However, the role of the patient to be compliant and be an active member of the diabetes management team cannot be over emphasized, and justifies major efforts to enhance diabetes education for these patients. Lastly, the large at-risk population of IGT individuals are offered a research program to determine if NIDDM can be prevented. The Diabetes Prevention Program is a five to seven year multi-center nationwide study to assess whether interventions of lifestyle changes and pharmacologic therapy can prevent diabetes among IGT individuals. As investigators in this Program, we seek our colleague's assistance in identifying these IGT individuals and working with us to possibly reduce the high prevalence of diabetes among Hawaiians and in the State of Hawaii.

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## External Ophthalmomyiasis, a Disease Established in Hawaii

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